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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,818	10/08/2003	Scott T. Weiss	B0801.70290US00	7475

23628 7590 10/12/2006

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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/681,818	**Applicant(s)** WEISS ET AL.
	Examiner Stephen Kapushoc	**Art Unit** 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12,54 and 111-134* is/are pending in the application.

4a) Of the above claim(s) *9-12,114,125 and 126* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,54,111-113,115-124 and 127-134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-12, 54 and 111-134 are pending.
Claims 9-12, 114, 125 and 126 are withdrawn.
Claims 1, 3-8, 54, 111-113, 115-124 and 127-134 are examined on the merits.

Election/Restrictions

1. Applicant's election without traverse of the invention of Group I (methods to assess sensitivity to a therapeutic), and the further election of the particular gene CRHR1 and the polymorphism rs1876828 (SEQ ID NO: 20) in the reply filed on 09/08/2006 is acknowledged. Only claims specifically reciting the elected polymorphism (SNP rs1876828) are examined, and they are only examined to the extent that they require the elected SNP; claims requiring the analysis of additional specific polymorphic positions are withdrawn.

Claims 9-12, 114, 125 and 126 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. The withdrawn claims require determining specific variation in the CRHR1 gene beyond the determination of the specifically elected rs1876828 SNP (SEQ ID NO: 20). For example, while the Election specifically elects only the particular polymorphism rs1876828, claim 9 specifically requires the determination of rs242939 in addition to the elected polymorphism (SNP rs1876828).

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. See for example pages 86-90 of the instant specification. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see for example page 88 of the specification). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4. The disclosure is objected to because of the following informalities:

Tables 9 and 10 contain the column headings 'BD848', 'Achr8', 'Preppch', and 'P848'. There does not appear to be any explanation or definition of these particular column headings.

Appropriate correction is required.

Claim objections

5. Claims 4, 7, 8, 54, 121-124, and 127-134 are objected to because they specifically recite non-elected subject matter. Claims 4, 7, and 8 specifically recite the determination of non-elected polymorphic position. Regarding claims 54, 121-124, and 127-134, while the specification indicates that SEQ ID NO: 20 and 240 contain the elected polymorphism (i.e. the SNP rs1876828), the claims specifically recite SEQ ID NOs that comprise non-elected polymorphic positions (e.g. SEQ ID NO: 14-19, 21-41, 205-208, 236-239, and 241-252). Applicant has elected for the examination of the claims in so far as they require the SNP rs1876828. Prior to allowance of any claims, the non-elected subject matter will be required to be deleted from the claims.

Claim Rejections - 35 USC § 112 2nd¶ - Indefiniteness

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 3-8, 54, 111-113, 115-124, and 127-134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-8, 111-113, and 115-120 are unclear over recitation of the phrase ‘the genotype of the subject is defined by a nucleotide sequence of a region of CRHR1’, because it is unclear if Applicant intends for the determination of a genotype of a particular nucleotide sequence, or merely a genotype variation that is in someway related to a different variation that is indicative of sensitivity. It is unclear what relationship is intended by the phrase 'is defined by'.

Claims 7 and 8 are unclear over recitation of the phrase 'the haplotype is defined by a nucleotide sequence', as it is unclear if Applicant intends to claim a method in which a haplotype comprising a particular polymorphic position is detected, or if some other relationship is intended by the phrase 'is defined by'.

Claims 4, 7, and 8 are indefinite over recitation of the term 'rs1876828' in reference to determination of a particular SNP because it is unclear if applicant intends for the claim to require the identification of particular nucleotide content at a specific position in a particular sequence context wherein the sequence context is that supplied by a database entry (for example a sequence associated with the rs1876828 entry in the NCBI SNP database), or the 629 bp sequence provided as SEQ ID NO: 20 (see for example page 37 of the instant specification), or the 53 bp sequence provided as SEQ ID NO: 240 (see for example page 77 of the instant specification).

Claims 4, 7, and 8 are indefinite over recitation of the term 'a polymorphism of rs1876828' because the indefinite article 'a' makes it unclear if applicant intends the claim to require the particular polymorphism, for example, as indicated at position 355 of SEQ ID NO: 20, or if any variation of SEQ ID NO: 20 is 'a polymorphism of rs1876828'.

Claims 54, 121-124, and 127-134 are unclear over recitation of particular nucleotide sequences and fragments as identified by (a) and (b) in claim 54. It is unclear if Applicant intends for (a) and (b) to further limit the 'nucleotide sequences of a region of CRHR1 which contains sequence variation', or if Applicant intends (a) and (b) to be alternatives to the 'nucleotide sequences of a region of CRHR1 which contains sequence variation' (e.g. thus reciting a Markush group with 3 elements).

Claims 54, 121-124, and 127-134 are unclear over the recitation of the phrase 'the fragments of the sequences' in part (b) of claim 54 as there is not proper antecedent basis for any particular 'fragment of the nucleotide sequences' in the claim.

Claims 54, 121-124, and 127-134 are indefinite because while the preamble of the base claim (claim 54) recites 'a method of assessing sensitivity to a therapeutic agent', there is no final process step that relates back to the purpose of the method as recited in the preamble. Thus it is not clear how the steps of the method as recited in the claim accomplish the purpose of the method.

8. Claims 1, 3-8, and 111-113, and 117-124 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The claims lack any particular method steps or processes such that the claims appear to require only the mental step of determining a genotype. For example the claims do not require obtaining a biological sample from the subject, or performing any processes to determine the genotype of the subject.

Claim Rejections - 35 USC § 112 1st¶ - Written Description

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-8, 54, 111-113, 115-124 and 127-134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

> Applicant is referred to the revised interim guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5, page 1099-111 (also available at www.uspto.gov).

The claims of the instant application are drawn to methods for assessing sensitivity to a therapeutic agent in a subject comprising determining a genotype of a subject wherein the genotype is defined by a variation in nucleotide content of a region of the CRHR1 gene. The claims broadly encompass the determination of any genotype comprising any sequence variation anywhere in a region of CRHR1, and further encompass the analysis of any organism possessing the CRHR1 gene. It is noted that while claims 4 recites the 'a polymorphism of rs1876828', the language of the claim makes does not limit the sequence variation to, for example, the sequence set forth as SEQ ID NO: 20 of the instant specification. Furthermore, claims 7 and 8 are drawn to any haplotype which minimally comprises 'a polymorphism of rs1876828'. And while claim 124 recites SEQ ID NO: 20 (as consonant with the election), the language of the claim which recites 'and fragments thereof' serves to broaden the scope of the claimed sequence variant beyond that disclosed as the A/G polymorphism at position 355 of SEQ ID NO: 20.

When the claims are analyzed in light of the specification, the instant invention encompasses the analysis of an enormous number of nucleic acid sequence variants, comprising a wide variety of sequences, wherein the variation in the sequence is indicative of therapeutic sensitivity. The instant specification provides that the term 'subject' broadly encompasses 'a vertebrate and preferably a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat or rodent' (page 14). Additionally, the specification provides that 'sequence variation' encompasses:

> At least one nucleotide in a nucleic acid which is different than a nucleotide in a reference nucleic acid. A reference nucleic acid is any nucleic acid having a known nucleotide sequence. Sequence variations include but are not limited to base pair substitutions, insertions, deletions, and splice variants (page 15).

Thus the claims encompass any variation (e.g.: any single or multi-nucleotide insertion, deletion, or substitution of any kind; any gene rearrangement or translocation; any splicing variant) anywhere within 'a region of CHRH1' (e.g. in any upstream enhancer element, promoter, 5'UTR, exon, intron, 3'UTR or downstream regulatory element), in any organism. For example, the Genecards output for CRHR1 (see provided output) indicates at least 167 SNPs in the human CRHR1 region (see pages 10-16 of the output). However, nucleic acids of such a large genus as encompassed by the claims have not been fully described.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. The specification provides only human sequences. In the instant case, the specification provides only the sequences of SEQ ID NO: 14-41, which provide the sequence context and nucleotide content of 28 SNPs in the CRHR1 gene, as well as SEQ ID NO: 236-252 which provide a shorter sequence context for 17 of the previously mentioned 28 sequences. The specification also provides SEQ ID NO: 205-208 as particular haplotypes in the CRHR1 gene, but does not appear to indicate which SNPs account for which particular positions in the disclosed haplotypes. The specification does not teach any other particular nucleic acid sequences or sequence variations in the genomic region encompassed by the claim.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other than nucleotide sequence or position within a particular gene), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, while the specification asserts that sequence variations in a region of the CRHR1 gene can be used to assess the sensitivity to a therapeutic agent, the specification provides only the 28 SNPs disclosed in SEQ ID NO: 14-41, and does not provide any teachings regarding how one might select any other additional sequence variants within the broadly claimed region that are indicative of sensitivity to a therapeutic in a human or any other organism. Thus the teachings of the specification do not provide guidance as to how one would a priori identify a nucleic acid sequence variant that is indicative of sensitivity to a therapeutic agent.

Applicants' attention is directed to the decision in In re Shokal, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the instant application, the several particular SNPs within the CRHR1 gene disclosed in the instant specification do not constitute an adequate written description of the broad subject matter of the claim, and so one of skill in the art cannot envision the detailed chemical structure of the sequences encompassed by the claims, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a statement that sequence variants within a particular ragion of a genome or with a particular functionality are part of the invention and reference to a potential method for their identification. The particular nucleic acid sequences are themselves required.

In conclusion, the limited information provided regarding particular SNPs as provided in the instant specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of the broadly claimed nucleic acids encompassed by the claimed methods. Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Claim Rejections - 35 USC § 112 1st¶ - Scope of Enablement

11. Claims 1, 3-8, 54, 111-113, 115-124 and 127-134 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> A method for assessing sensitivity to a therapeutic agent in a human subject with COPD or asthma, wherein the subject is an adult Caucasian, and wherein the therapeutic agent is Triamcinolone, and wherein sensitivity is determined by an increase in FEV_1, the method comprising:
> obtaining a biological sample from the subject, wherein the biological sample contains nucleic acid encoding the CRHR1 gene;
> determining the genotype of the subject in both copies of the CRHR1 gene by determining the sequence content at nucleotide position 355 of SEQ ID NO: 20 in both copies of the subjects CRHR1 gene;
> and making an assessment of sensitivity based on the genotype of the subject where a subject homozygous with an AA genotype is more sensitive to the therapeutic agent than a subject with a heterozygous AG genotype or a homozygous GG genotype,

does not reasonably provide enablement for the analysis of any non-human subjects, or subjects other than adult Caucasians with COPD or asthma, or any therapeutic other than Triamcinolone, or the assessment of any risk factors, or any assessment other than the AA genotype being associated with increased sensitivity and the AG and GG genotypes being associated with decreased sensitivity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Many of the rejected claims are generic with regard to the nucleic acid sequence variation that is determined in the claimed method. While there may be other enabled specific embodiments of analyzed polymorphic positions, consonant with the Election only methods specifically requiring the particular analysis of rs1876828 (SEQ ID NO: 20 and 240) were considered. All data was considered for the analysis of the generic claims.

Nature of the invention and breadth of the claims

The claims of the instant invention are broadly drawn methods for assessing sensitivity to a therapeutic agent by determining the presence of a nucleotide sequence variation in a subject in a region of the CRHR1 gene.

The claims encompass the analysis of any subject organism, and any measure of sensitivity to any therapeutic agent. The claims further encompass the analysis of any sequence variation anywhere with a region of CRHR1 in the subject's genome.

Claim 4 requires the detection of a SNP that comprises any polymorphism of rs1876828.

Claims 7 and 8 require detection of any haplotype comprising a polymorphism of rs1876828.

Claim 124 encompass detection of any sequence variation in any fragment of SEQ ID NO: 20.

Claims 119, 120, 133 and 134 require the analysis of additional risk factors in the determination of therapeutic sensitivity.

Claims 113 and 123 require determining the sensitivity to any therapeutic agent in a subject suffering from depression.

The nature of the invention requires knowledge of a correlation between genotype of sequence variants in the CRHR1 gene and sensitivity to therapeutic agents.

Direction provided by the specification and working example

The instant specification provides an analysis of the association between nucleotide content at specific single nucleotide polymorphism (SNP) positions in the CRHR1 gene and sensitivity to different inhaled corticosteroids in different populations. The specification provides (see summary page 83 of specification) an analysis of:

i) an adult population (Adult Study/Forest) using Flunisolide
ii) a pediatric population (CAMP) using Budenoside
iii) an adult population (ACRN) using Triamcinolone

The specification indicates that due to concerns regarding population stratification, only genotypic information from Caucasions were analyzed (page 83). The specification provides only the analysis of these subjects suffering from asthma related respiratory disorders.

The specification does not teach the analysis of subjects taking any other particular corticosteroids or any other therapeutics, nor any subjects suffering from any other particular health issue, such as depression.

The specification teaches that in the adult population taking Triamcinolone, subjects homozygous AA at position 355 of SEQ ID NO: 20 had a higher average increase in their FEV_1 in response to Triamcinolone than subjects heterozygous AG or homozygous GG at the position (page 84, Fig 4B).

The specification does not teach any other nucleotide content at the particular position. Nor does the specification teach any significant correlation between nucleotide content at the position and sensitivity to Flunisolide or Budenoside in the analyzed populations.

The specification does not teach the analysis of any risk factors with regard to prediction of therapeutic sensitivity based on CRHR1 genotype.

The specification teaches four haplotypes within the CRHR1 gene (page 71, SEQ ID NO: 205-208), but the specification does not indicate which SNP positions from the CRHR1 Gene correspond to which particular positions within the provided haplotype sequences. The specification does not indicate the nature of the nucleotide content at the elected SNP position (i.e. position 355 of SEQ ID NO: 20) in any other haplotypes, nor how any other haplotypes are associated with sensitivity in the Flunisolide or Budenoside populations, nor any analysis of haplotypes in the Triamcinolone population.

State of the art, level of skill in the art, and level of unpredictability

While the state of the art and level of skill in the art with regard to the detection of any particular genotype, or the detection of a particular polymorphic form of a genotype, is high, the level of unpredictability with regard to associating the presence of a particular genotype or polymorphic form of a genotype with any phenotype, such as sensitivity to any therapeutic, is even higher. The unpredictability is demonstrated by the prior art, the post filing art, and the instant specification.

While the claims encompass the analysis of any subject organism, the specification provides no analyses other than of human subjects. It is thus highly unpredictable as to whether or not detection of any particular nucleotide content in a region of CRHR1 will be indicative of therapeutic sensitivity in any other organism.

While the claims encompass the assessment of sensitivity to any therapeutic, the instant specification indicates the unpredictability with regard to the sensitivity of individuals with different genotypes to different therapeutics. For example, while the specification indicates that the sensitivity of a subject to Triamcinolone can be determined by analysis of the nucleotide content at position 355 of SEQ ID NO: 20 (Fig 4B and page 84), the specification provides so such correlation with regard to Flunisolide (see Tables 3, 4, 7 and 8) or Budenoside (see Tables 5 and 6). It is thus unpredictable as to how one might extrapolate data regarding genotype:sensitivity associations regarding one therapeutic to any other therapeutic.

Additionally, while the claims encompass the analysis of both pediatric and adult subjects, the instant specification indicates the unpredictability with regard to predicting therapeutic sensitivity in different populations based on genotype. For example, while Fig 4B indicates that the rs1876828 polymorphism is associated with therapeutic sensitivity in an adult population, no such association is seen in a pediatric population (Tables 5 and 6).

And while the claims encompass the detection of any variation in any nucleotide sequence in a region of CRHR1, it is relevant to indicate that the instant specification teaches an analysis of only s2 specific SNPS in the human CRHR1 gene (SEQ ID NO:

14-41). Genecards output for CRHR1 (see provided output) indicates at least 167 SNPs in the human CRHR1 region (see pages 10-16 of the output). However, the specification does not indicate any association between nucleotide content and therapeutic sensitivity for most of these SNPS. It is thus unpredictable how any of the many different mutations encompassed by the claims would be used to predict therapeutic sensitivity.

And while the claims encompass the use a haplotype defined by the elected polymorphism, the specification does not clearly indicate that the elected polymorphism is in fact a defining element of haplotype associated with sensitivity to a therapeutic. For example, the specification teaches only four CRHR1 haplotypes comprised of 17 particular markers (page 71). The specification does not indicate which markers are which positions of the disclosed haplotypes. The specification asserts that three SNPs allow for delineation of the four haplotypes (p.84). However it is unclear that the SNP chosen in the election is in fact consistently and significantly indicative of sensitivity to a therapeutic. For example, it appears form the instant specification (Table 14) that a G at the elected position can be associated with two haplotypes, GAT and GGT, defined by rs1876828, rs242939, and rs242941. However the GGT haplotype does not appear to be indicative of sensitivity in the Forest population. Additionally, the post-filing art of Licinio et al (2004) indicates the presence of a GAG haplotype in a human population (p.1075 – Abstract), but the instant specification does not teach any such haplotype. Additionally, the specification teaches that an A at rs1876828 is associated with an AAG haplotype, but such a haplotype is not significantly (i.e. $p>0.5$) associated with therapeutic sensitivity in an adult population. Given the breadth of claims requiring the use of rs1876828 to identify a haplotype wherein the haplotype is indicative of therapeutic sensitivity, it is highly unpredictable as to how one might use the elected SNP to assess sensitivity.

Additionally, while the claims encompass the analysis of subjects with depression, it is relevant to point out that the instant specification provides no such analysis. And while the post filing art of Licinio et al (2004) indicates that a particular haplotype must be detected to determine response to fluoxetine and despramine (Table 3), the reference does not indicate that the particular SNP rs1876828 is significantly associated with sensitivity (p.1079, right col., first full paragraph). Additionally, the instant specification does not specifically contemplate the particular methods of the reference (e.g. sensitivity to the particular therapeutic in the specific patient population using the particular haplotype) and thus the instant specification is not considered enabling for the analysis methods of the reference.

Quantity of experimentation required

A large and prohibitive amount of experimentation would have to be performed in order to determine if it is even possible to make and use the invention in the full scope of the claims. While one of skill in the art could carry out experimentation aimed at identifying other polymorphisms and haplotypes in CRHR1 that are associated with therapeutic sensitivity, the outcome of such experimentation can not be predicted, and it is in fact unknown whether any quantity of experimentation would be sufficient to more broadly enable the claimed invention. Such experimentation would require determining the predictive value of any sequence variation in any genomic region of CRHR1 and how it is associated with any sensitivity to any therapeutic. This would require the analysis of an enormous number of subjects with a wide variety of genotypes as well as subject response to any therapeutic needed for any reason. Even for the particular case of the elected SNP, one would have to analyze any haplotype in which the SNP can be found, and analyze different populations (e.g. different ages and races) to examine the response to any different therapeutic.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and the breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the amount of guidance by the applicant and the specific working examples, it is the conclusion the an undue amount of experimentation would be required to make and use the claimed invention in the full scope of the claims.

Claim Rejections - 35 USC § 102

In the rejection of claims under 35 USC 102 the requirements of the claims are noted. The claims require only the determination of a genotype in a subject, wherein the genotype comprises a sequence variation indicative of sensitivity to a therapeutic agent.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 3, 4, 54, 117, 118, 124, 130, 131 and 132 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank GI:11128430 (2000).

GenBank GI:11128430 teaches the nucleic acid sequence of a genomic clone obtained by sequence analysis of a clone HCIT104N19. The process of sequence analysis is thus a method for determining a genotype or detecting the presence of a nucleic acid satisfying the limitations of the rejected claims. For example, the reference teaches the detection of a G at position 26 of SEQ ID NO: 240 (see positions 58,971 – 59023 of the sequence of the reference).

Relevant to claim 1, the reference teaches the determination of a G at position 26 of SEQ ID NO: 240 (see positions 58,971 – 59,023 of the sequence of the reference; see also provided Align 11128430 : SEQ ID NO: 240). The G at position 26 of SEQ ID NO: 240 is inherently associated with decreased sensitivity to Triamcinolone in a human adult Caucasian population.

Relevant to claims 3 and 4, the detected G at position 58,996 is a single nucleotide polymorphic position.

Relevant to claim 54, the reference indicates the detection of the nucleic acid encompassed by SEQ ID NO: 240, as required by the claim, wherein the presence of a G is inherently indicative of decreased sensitivity to Triamcinolone in a human adult Caucasian population.

Relevant to claims 117 and 118, the G at position 58,996 is inherently associated with decreased sensitivity to the corticosteroid Triamcinolone.

Relevant to claim 124, the reference teaches that positions 58,971 – 59,023 are equivalent to SEQ ID NO: 240, which is a fragment of SEQ ID NO: 20.

Relevant to claim 130, the reference teaches obtaining the sequence of a clone from human chromosome 17, which is genomic DNA.

Relevant to claims 131 and 132, the G at position 58,996 is inherently associated with decreased sensitivity to the corticosteroid Triamcinolone.

Relevant Art Cited

The enabled data presented in the instant application was presented at the 53rd Annual Meeting of the American Society of Human Genetics. Los Angeles, CA, USA. November 04-08, 2003, as evidenced by the provided abstract and citation information. The earliest date of the meeting (i.e. 11/04/2003) falls after the filing date of the instant application (i.e. 10/08/2003).

Conclusion

14. No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Kapushoc
Art Unit 1634

DIANA JOHANNSEN
PRIMARY EXAMINER